# Iatroplacebogenesis: a useful therapeutic tool?

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**The placebo effect is ubiquitous, being present in every patient–treatment situation. In the era of prescientific medicine, the reputation of healers was built largely upon the power of this effect. In modern medicine the effect continues, and may be harnessed to enhance sound scientific treatment and thus facilitate recovery.**

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As Sir William Osler once said:

> **'The desire to take medicine is one feature which distinguishes man, the animal, from his fellow creatures. It really is one of the most serious difficulties with which we have to contend' (Osler, 1894).**

From time immemorial, man has felt the need to self-medicate, and to seek help from healers in times of mental and physical distress. In the days of prescientific medicine, the pills, potions and procedures dispensed by healers were seldom pharmacologically active. When preparations did contain active ingredients, they were potentially harmful to those ingesting or applying them. Details of such preparations are to be found in any text on the history of medicine, and include such items as frog sperm, crocodile dung, dried viper lozenges, oil of ants, moss scraped from the skulls of victims of violent deaths and eunuch fat (Shapiro, 1971).

Despite the administration of such bizarre prescriptions, physicians and other healers maintained a position in society which was then (as now) prestigious and of high esteem. Their success was due to two phenomena which worked in harmony towards the achievement of human recovery: first, the human homeostatic propensity, which was directly responsible for the self-limitation of many pathologies, and second, the powerful and ubiquitous placebo effect. This second effect may indeed be thought of as an extension of the first. Thus the placebo effect has the potential to facilitate the ability to self-heal which lies within us all.

## Pleasing the patient

The word placebo stems from the Latin *placere* which means 'to please'. One of the earliest occurrences in medical literature is recorded in *Hooper's Medical Dictionary* in 1811, where it was described as:

> **'...an epithet given to any medicine adopted more to please than to benefit the patient.'**

The tone of this definition captures the faint air of disapproval with which placebo administration was (and to a large extent still is) viewed by the medical profession.

However, even four decades ago, when the word 'placebo' first appeared in the title of a medical paper (Wolf et al, 1946), it had its protagonists. The authors objected to the definition given above, arguing very reasonably that if a patient is pleased, then he is also benefited by his treatment — an early acknowledgement, perhaps, of the importance of consumer satisfaction in the presentation of clinical treatment.

Placebo has been redefined in medical literature many times. A useful, neutral definition is offered by Shapiro (1971):

> **'...any therapy, or that component of any therapy, that is deliberately used for its non-specific, psychologic or psychophysiologic effect, or that is used for its presumed scientific effect on a patient, symptom or illness, but which, unknown to patient and therapist, is without specific activity for the condition being treated.'**

In this analysis, Shapiro extends the definition beyond the commonly held view, i.e. the administration of a sugar pill by the knowing doctor to the ignorant patient, to one that is broader in its perspective. The term now also includes any therapeutic procedure which is assumed by both patient and therapist to be specifically active in relation to a particular problem, but which, in reality, cannot and does not have any specific effect upon the condition being treated.

## The ubiquitous placebo effect

This perspective was enlarged upon by Epstein (1984) when he stated:

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*'At the point when scientific medicine was born, the holistic, consumer-oriented approach to medical management suffered a demise. The art of medicine was largely lost as the science of medicine was delivered. The preoccupation of doctors now lay with the patient as a medical condition, rather than the patient as a person.'*

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**'The placebo effect also occurs with all active or real treatments'.**

The placebo effect is ubiquitous (Abel, 1991). Every time there is a clinical encounter between doctor or therapist and patient, the placebo effect forms part of that encounter.

Thus the history of prescientific medicine was primarily the history of the placebo effect. With the advent of scientific medicine, former quackeries were recognized as such, and were rapidly cast into disrepute. There was a complete metamorphosis of medical opinion, catalysed by the germ theories of Pasteur and Koch:

> **'They imposed upon medical thought; they transfixed its theoretical and philosophical corpus with the vivid concept of the specific aetiological factor, and by necessity also with its corollary, the specific antidotal curative agent' (Galdston, 1954).**

Every disease was therefore seen to stem from a specific cause, which necessitated treatment by a similarly specific agent. Treatment was demanded by the patient and administered by doctors.

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But what of the powerful placebo effect? Had it been 'switched off' as it was superseded by the new era of modern medicine? Testimony to the continued existence of the phenomenon came from controlled drug studies, which were initiated from the 1950s. However, the placebo effect was not considered a useful one at this time, being viewed with disfavour as a potential contaminant of research findings.

## How effective is placebo?

When making a quantitative assessment of placebo effectiveness it is necessary to look at both the types of condition and also the number of patients within any treatment group who may have their symptoms eased or alleviated by placebo administration. The use of a placebo control in clinical trials has produced a wealth of information in these areas. Thousands of medical papers include the word 'placebo' in their title. There are too many of these to even begin to list here, but reference to this body of material will demonstrate that the placebo response is efficacious in facilitating recovery at a statistically significant level in a wide variety of disparate conditions. These include surgical pain, gastric ulceration, hypertension, diabetes, nausea, clinical anxiety and depression, status asthmaticus, schizophrenia, arthralgia, cancer, tinnitus and the common cold.

There are very many more examples. Indeed, Haegerstam et al (1982) stated that:

> **'Nearly every organ system in the body can respond to placebo treatment.'**

A characteristic level of efficacy for the placebo response was identified in the 1950s by Beecher:

> **'It is evident that placebos have a high degree of therapeutic effectiveness in treating subjective responses, decided improvement, interpreted under the unknown technique as a real therapeutic effect, being produced in 35.2 ± 2.2% of cases. This is shown in over 1000 patients in 15 studies covering a variety of areas...'**

The value of 35% efficacy in producing a therapeutic effect has been observed many times since in clinical trials. However, the placebo effect can be considerably greater than this under the appropriate conditions. Spiro (1986) noted that in double-blind controlled trials conducted in patients with duodenal ulceration, 50–60% of ulcers healed with placebo therapy, whereas about 70% healed with a specific drug treatment. However, there is no absolute value of placebo response for every individual condition. Spiro reported differences in healing rates for duodenal ulcer craters, ranging from 20% in London to 70% in Switzerland for patients receiving placebo therapy. He also cited an identical drug trial carried out in London and Dundee, where the efficacy of the placebo response in achieving healing of known duodenal ulcer craters was 44% in London compared with 74% in Dundee. Reasons for this variation in placebo response rate remain unclear.

Beecher (1955) noted that 75% of a patient group in severe post-operative pain had their symptoms relieved by a large dose of morphine, whereas 35% achieved the same level of relief from a normal saline placebo. He reasoned that:

> **'The placebo effect of active drugs is masked by their effects. The power**

**attributed to morphine is then presumably a placebo effect plus its drug effect. The total "drug" effect is "active" effect plus its placebo effect' (Beecher, 1955).**

According to Beecher, half of the effect of a postoperative injection of morphine may be accounted for by the placebo response. It may therefore be deduced that placebo therapy can be half as powerful as morphine in producing relief from pain (*Table 1*).

Is it not extraordinary that a clinical tool which has been shown to be both wide ranging and potent in its effectiveness should be so under-utilized in the treatment of patients? Price (1984) expresses a similar puzzlement:

**'If the pharmaceutical industry were to produce a drug which was as reliable, of such wide ranging applicability and with a record of efficacy as impressive as that of the placebo effect, it would no doubt be proclaimed a miracle panacea, and attributed to the wonders of science.'**

Table 1. Relationship of placebo component effect to total drug effect

| | | | | |
|---|---|---|---|---|
| Drug effect | = | active ingredient effect | + | placebo effect |
| Drug effect (This is the classic 'clinical trial') | – | placebo effect | = | active ingredient effect |
| Drug effect | – | active ingredient effect | = | placebo effect |
| In the Beecher trial (1955) Drug effect at 75% | – | active ingredient effect at 35% | = | placebo effect at 30% |

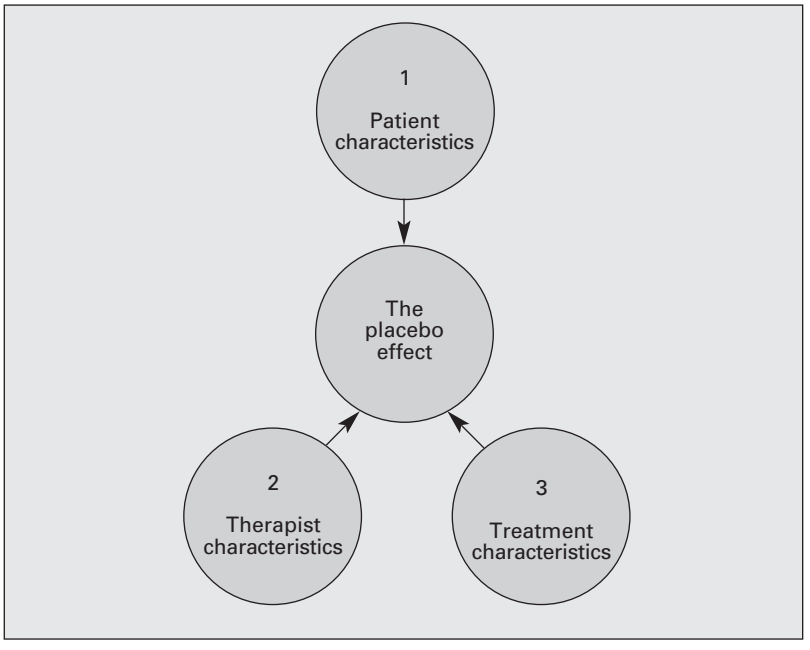


Figure 1. Component factors which may generate the placebo effect.

## Factors generating the placebo response

Having identified the potential potency of the placebo effect in terms of both numbers of patients and variety of conditions likely to respond, the next step is to identify the factors involved in initiating this effect (*Figure 1*).

Such factors may be divided into three main categories:

- Characteristics of the patient
- Characteristics of the doctor/therapist
- Characteristics of the treatment situation.

## Who responds to placebo?

A plethora of information exists concerning the personality and social characteristics of the placebo responder. Evidence is either non-conclusive or conflicting, and the general consensus is that there is no set of predictors which accurately describe a potential placebo responder (Gowdey, 1983; Reimherr et al, 1989; Lanvin, 1991; Wall, 1993; Turner et al, 1994).

It seems that anxious patients respond well to placebo (Wolf, 1959; Moertel et al, 1976; Fields and Levine, 1981; Bech, 1989), but in each case this is related to a particular emotional state stemming from stress (probably largely caused by their illness and not a habitual personality trait).

It seems that all persons, subject to suitable environmental conditions, might exhibit a positive response to placebo. However, the response is so variable that there will be no greater likelihood than may be described by chance that a person who responds to placebo in one situation will respond in another, even in the course of the same study (Beecher, 1955; Moertel et al, 1976; Lasagna, 1979; Brody, 1980; Wall, 1993). Thus, although 30–50% of a population are likely to respond to placebo in a variety of situations, it will not always be the same people who will be responders or non-responders.

Although no consistent findings have emerged to identify a 'placebo personality', many medical personnel express a common prejudice in their opinion of the person most likely to react to a non-specific treatment. Vogel et al (1980), for example, state:

**'A common opinion among physicians is that only individuals who are psychologically defective, neurotic, suggestible, hysterical, over-reactive or weak willed will respond to placebo — that is, there must be something wrong with a person if he responds to placebo.'**

*'Evidence indicates that the patient who responds to placebo has a high level of pain or other clinical need about which they are anxious, has the capability for self-help and mastery, and has enjoyed favourable experiences in the hands of health professionals in the past...'*

Evidence indicates that the patient who responds to placebo has a high level of pain or other clinical need about which they are anxious, has the capability for self-help and mastery, and has enjoyed favourable experiences in the hands of health professionals in the past (Brody, 1980; Shapiro et al, 1980; Levine et al, 1981; Olsson et al, 1989). Thus a placebo responder can be described as a patient whose need is great, and whose faith in the ability of health-care professionals to provide assistance is also great.

These findings contrast sadly with the opinions that medical staff are likely to hold about such patients. Goodwin et al (1979) cite a quote from a senior resident on his perception of placebo use:

> **'Placebos are used with people you hate, not to make them suffer, but to prove them wrong.'**

Thus it is the patient with the greatest need and the greatest faith who is likely to respond, but if medical staff discover that a patient has responded in this way, then they are likely to despise the patient for that response and assume, quite incorrectly, that their symptoms must have been imaginary (Kapp, 1983).

## Who elicits the placebo response?

In the Western world, people who occupy healing roles, whether they be doctor, physiotherapist, herbalist or osteopath, are popularly endowed with a much higher status than their abilities deserve (Doongaji et al, 1978; Totman, 1979; Zimba and Buggie, 1993). This can lead to unrealistic expectations among patients about healers' capacity to effect a cure (Galdston, 1954; Gryll and Katahn, 1978).

The environment in which health service personnel operate can further contribute to the mystique, acting as a stage setting in which the therapeutic interaction takes place. This setting is filled with insignia of the healing process: expensive equipment, documentation involving strange symbols, the presence of other sufferers of physical ailments also seeking help, and a general pervasive sensation of strangeness engendered by unusual smells, sounds and sights. A patient may enter such an environment with a need for help and an expectation that this will be provided — factors which may predispose them to a positive placebo response.

In addition to the predisposing factors that a patient brings with him/her into a health-care environment, factors associated with the therapist have the capacity to increase a patient's ability to self-heal. Key factors in the interaction between the therapist and patient which are asserted with a placebo response are warmth and social support, status, empathy, provision of information, overt interest in the patient and his condition, and, most importantly, the capacity to generate positive expectations of outcomes (Buchalew, 1972; Beck, 1977; Brody, 1980; Lyno, 1990). Thus patient factors may combine with therapist factors to activate the placebo effect. This is the important process of iatroplacebogenesis.

Gryll and Katahn (1978) attempted to quantify some of these factors. They summarized their findings as follows:

> **'Each of the four independent variables investigated (status of placebo administrator, attitudes of dentists and dental technicians towards the patient and the type of message about the expected drug effects) affected the patient's responses to placebo administration: the most salient of the four variables was the type of information contained in the message of drug effects...The importance of the status variable emerged only within the interplay among the four situational variables under investigation'.**

Thus the healer who is most likely to activate the placebo response in a patient will be one who combines competence and confidence with a warm and caring attitude towards the patient, and who gives implicit and explicit positive communication concerning expected treatment outcomes (Lehrman, 1993; Wall, 1993) (*Figure 2*). This illustrates the great paradox concerning iatroplacebogenesis (Shapiro, 1969), i.e. that it is the most proficient administrator of specific physical treatments who will engender the greatest placebo effect. This in turn can supplement the already sound clinical procedure to maximize the beneficial outcome of treatment.

However, if negative statements which express doubt are made, by personnel who express little warmth or interest in the patient, the placebo effect may be actively noxious, working against scientific treatment to produce deleterious treatment outcomes (Wolf, 1959; Wickrameskera, 1980; Fields and Levine, 1981; Butler et al, 1983; Barrie, 1984). When summarizing the results of an experiment conducted into the efficacy of certain tranquillizing drugs,

where the degree of enthusiasm for the product by the doctor utilizing it was included in the study details, Wolf (1959) wrote:

> **'The correlation showed that those patients that had done best were in the group treated by the doctors who like the drug best. Those who did poorly were patients of the therapeutic nihilists.'**

Figure 2. Combining competence and confidence with a warm and caring attitude.

Figure 3. The key feature of a treatment which will trigger the placebo response is an ability to impress the patient with its potential potency as a healing agent.

## Which treatments generate a placebo effect?

Because most of the information in this area has been obtained from clinical drug trials, much of the research evidence is concerned with the manner in which a drug is administered, in terms of method of administration, colour, size and dosage (Shapira et al, 1970; Evans, 1974a; Huskisson, 1974; Buchalew and Coffield, 1982).

It was two decades ago that Lasagna (1979) noted that a drug could have a variable placebo effect depending upon its characteristics. He found the placebo effect to be greatest when tablets were either very large or very small, and suggested that the large tablets impressed by sheer size, while the small ones impressed by their assumed potency.

Treatments that are unpleasant, either because of their taste (Evans, 1974b) or their side-effects (Thomson, 1982), can also act as potent placebos. Perhaps, like the witches' brew, the medicaments present as being so unpleasant that they are perceived as being very powerful.

In each case, it can be argued that the key feature of a treatment which will trigger the placebo response is an ability to impress the patient with its potential potency as a healing agent (*Figure 3*). Once again the key process is the generation of expectations of success in terms of treatment outcome.

Overall, the more specialized, fashionable, powerful, costly and complex a patient perceives a treatment to be, the stronger will be the placebo effect which runs alongside and reinforces that treatment (Beck, 1977; Lasagna, 1979; Buchalew and Ross, 1981). Hence open heart surgery is likely to be more active in its non-specific effects than a less major operation, intermittent traction given on expensive equipment more active than manual traction, and a drug given by injection more active in its non-specific effects than the same drug given in tablet form (particularly if the tablet is white and of medium size).

## The potential of placebo

The placebo effect will therefore be greatest when patients who have severe clinical problems approach clinicians in whom they have great faith. If those clinicians are clearly interested in their case, have a warm and caring attitude, are willing to listen, give them information and specialized

treatment, and above all engender the expectation that they have the capacity to help the patient, then there is a very strong possibility that the placebo effect will be activated in a positive direction.

The placebo effect forms part of every interaction between patient and clinician. If utilized wisely it may supplement and enhance scientific medical procedures and substantially increase their effectiveness. If abused it may operate against such treatments and actively reduce their efficacy. Medicine as art and medicine as science operate harmoniously when the placebo effect is utilized with insight to reinforce a scientific treatment procedure. In this manner, the capacity for self-healing which resides within us all may receive maximal stimulation.


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## KEY POINTS

- **The placebo effect operates to facilitate the process of self-healing.**
- **It can be effective at a significant level in all body systems.**
- **It is present in every patient–treatment situation.**
- **It works best with patients who are most ill.**
- **Used wisely, it will supplement and complement the scientific effects of all treatments.**